among the growing list of causes of nontraumatic rhabdomyolysis and myoglobinuria.

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Malignant Pseudomonas External Otitis

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MALIGNANT PSEUDOMONAS EXTERNAL OTITIS is a severe, necrotizing, external ear canal infection most often occurring in elderly persons with diabetes mellitus. It is accompanied by high complication and mortality rates.[1] Early diagnosis and therapy can circumvent the complications of cranial nerve palsies, osteomyelitis of the skull, meningitis, parotitis, vascular thrombosis, septicemia and death. A primary care physician usually first sees a patient with the disease but, because of few descriptions of the disorder in the general medical literature,[2-5] he may not be completely familiar with the presentation and complications. Therefore, we report the case of a patient who was cured without complications by parenteral administration of antibiotics and appropriate surgical therapy. The literature also is reviewed.

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Report of a Case

The patient, a 70-year-old white man, had been treated uneventfully for diabetes mellitus with chlorpropamide for four years. One week before admittance to hospital, the patient presented to a general medical clinic with pain in both ears. Treatment was begun with local administration of drops (polymyxin B, bacitracin, neomycin, hydrocortisone) and orally given phenoxymethyl penicillin for bilateral external otitis. The pain in the right ear resolved but a painful purulent discharge continued from the left ear. Despite wick packings and topical therapy with antibiotics (colistin, neomycin, thonzoniumbromide, hydrocortisone), the condition progressed to ulceration of the floor of the left external canal. This condition was accompanied by a small polypoid mass with the gross appearance of granulation tissue. Pure cultures of Pseudomonas aeruginosa were obtained twice. A biopsy specimen of the polypoid mass showed granulation tissue with no evidence of malignancy. Because of the unresponsiveness of the lesion to treatment, the culture results and the history of diabetes, the patient was admitted to hospital with a diagnosis of malignant Pseudomonas otitis externa so that parenteral administration of antibiotics could be begun.

On admission an ulcer was noted on the floor of the canal of the left ear at the juncture of the membranous and cartilaginous portions and there was purulent discharge and pronounced tenderness over the mastoid. An audiogram documented a mild, left sensorineural hearing loss at 2,000 to 8,000 Hz. Findings on x-ray studies of the mastoid showed slight clouding. Probing of the ear dis-

closed a deep sinus tract that extended at the junction of the membranous and osseous portion of the external canal back to the still intact, bony roof of the mastoid. Chondritis was present to the level of the mastoid roof.

A regimen of gentamicin was begun, 70 mg given intramuscularly three times a day, and gentamicin otic drops. Because there was no improvement, administration of carbenicillin, 24 grams per day, was begun 13 days after the gentamicin was given. Following a ten-day course of carbenicillin and a 26-day course of gentamicin, the lesion healed. However, four days following discontinuation of the antibiotics, the purulent left ear drainage recurred. Pseudomonas aeruginosa was cultured again; repeat x-ray studies of the mastoid showed improved aeration compared with findings on the previous studies. Intramuscular administration of gentamicin, 70 mg per kg of body weight per day, and intravenous therapy with carbenicillin 30 grams per day, were reinstituted. Five days later extensive debridement of the entire external canal was carried out. No bone involvement was found. Gentamicin drops were given locally and there was gradual and uneventful wound healing. There were no recurrences, middle ear involvement or cranial nerve palsies. Cultures for acid-fast bacilli and fungi were all negative.

Discussion

There are two distinctly different ways in which Pseudomonas infects the external ear canal. The most common condition, frequently referred to as swimmers' ear or simple external otitis, is a mild infection, usually seen in children. It responds to local therapy without sequelae. This relatively benign form of external otitis should be clearly differentiated from malignant Pseudomonas external otitis which occurs primarily in elderly diabetic patients and is associated with multiple complications including hearing loss, cranial nerve palsies, parotitis, osteomyelitis, intracranial vascular thrombosis, meningitis, septicemia and, in a high percentage of patients, death. The first description of this process was in 1959.[6] Since then experience with approximately 127 cases has been described in the English language literature[1-25] and several additional cases have been reported in the foreign literature. Chandler, who originally coined the term malignant Pseudomonas external otitis in 1968,[1] has had the largest single experience with the disorder. In 1977 he updated his observations, while describing in detail the complications of sigmoid sinus thrombosis and secondary mastoiditis.[24] With the exception of four instances,[2-5] all reports of this disease have been published in the ear, nose and throat, and the neurological literature.

Except for 15, all of the 127 cases have involved patients with some form of diabetes, ranging from mild abnormalities of glucose tolerance to overt, insulin requiring disease. The ages of the patients have ranged from 7 months to 91 years (with an average age of 70 years). A sex or race ratio cannot be determined accurately, although it appears that Caucasians have predominated.

At first the infection is relatively inconspicuous. Gradually it worsens, and a painful, purulent discharge from the external canal develops. Occasionally, minor trauma has precipitated the infection. One case, for example, was associated with trauma from a hearing aid and one with lancing of an external canal furuncle.[1] Another occurred "after removal of a piece of hard wax with some flesh attached."[11] Except for those three instances, no specific initiating event or clinical circumstance has been defined.

After the process becomes established its appearance is so characteristic that it deserves special comment. The purulent drainage is associated with a polypoid mass of granulation tissue at the juncture of the membranous and osseous portion of the external canal. Accompanying findings have been mastoid tenderness, stenosis of the external canal, periauricular cellulitis, contiguous involvement of the tympanic membrane and hearing loss.

Kim,[9] in his review of x-ray findings in this disorder, pointed out the value of ear tomograms to assess the extent of involvement of the initial process. Early features of extension to bone included clouding of the middle ear cavity, destruction of the lateral attic wall, and destruction and dislocation of the ossicular structures. In late stages destruction of the tegmen and jugular foramen and extension to the petrous apex were shown on x-ray films.

Three directions of extension from the original external canal site have been reported: (1) toward the middle ear, (2) inferiorly and posteriorly into the mastoid air cells and (3) anteriorly into the parotid gland and tempromandibular joint. Ultimately, in many cases infection extends into the intracranial cavity. Associated with this

extension from the external canal focus has been a high incidence of cranial nerve palsies; the facial nerve is most frequently affected by extracranial encroachment at the stylomastoid foramen.

Dinapoli and Thomas[2] in their review of the neurological complications noted that the 7th, 10th, 11th, and 12th cranial nerves were the most frequently involved early in the disease's course in their patients. In contrast, the nerves involved later were the 3rd, 5th and 6th. Involvement of the 10th, 11th and 12th was a complication of osteomyelitis at the base of the skull near the jugular and hypoglossal foramina. The involvement of the 3rd, 5th and 6th cranial nerves was considered to be a result of progressive osteomyelitis, but concurrent meningitis or spread through the internal carotid artery and its branches could not be ruled out. Although multiple cranial nerve involvement is generally associated with a poor prognosis, in one report a patient with multiple palsies survived with only minimal residua.[18]

In Chandler's 1977 report, he reviewed his experience with this external ear disease in 72 patients.[24] He emphasized the reduction of morbidity and mortality that has accompanied an increased awareness of the potential seriousness of the infection, the institution of carbenicillin and gentamicin therapy, and an increased surgical aggressiveness when appropriately indicated during failure of medical treatment. In addition, he expanded the literature on the complication of sigmoid sinus thrombosis by describing four cases of proven thrombosis and another seven of suspected thrombosis. Although in most of these cases there was clinical involvement of the nerves leaving the jugular foramen, in one patient sigmoid sinus thrombosis was shown during surgical operation and there were no cranial nerve deficits. In addition, in this review, Chandler pointed out the complication of mastoiditis without middle ear involvement and suggested that whenever the diagnosis of malignant Pseudomonas external otitis is made a series of x-ray studies of the mastoid should be done early. He described several cases of mastoid involvement which responded to carbenicillin and gentamicin therapy, making surgical drainage unnecessary.

A relatively clearly defined approach to patients with malignant Pseudomonas external otitis can be developed from a review of the literature. The initial therapy should consist of topical administration of antibiotics (gentamicin wick packing). If response is not rapid, local debridement should be undertaken and the diagnosis of malignant Pseudomonas external otitis considered if cultures are positive for Pseudomonas. Cultures of the granulation tissue with full sensitivities of the organism should be done because of an emerging resistance of Pseudomonas to gentamicin. If improvement does not occur, intravenous administration of carbenicillin and gentamicin should be instituted. Although the experience is limited, tobramycin[19] or amikacin should be an acceptable alternative to the gentamicin; ticarcillin[19] should be an acceptable substitute for the carbenicillin. If the response is less than optimal, appropriate surgical debridement should be undertaken. Early diagnosis and parenteral administration of antibiotics, combined with appropriate surgical therapy, are necessary for minimizing disfiguring and potentially fatal complications.

Summary

Since 1959, when the first case of malignant Pseudomonas external otitis was described, approximately 127 cases have been reported in the English language literature. Diabetes has been present in 88 percent of the patients. The average age has been 70 years.

A typical presentation includes a chronically infected external ear canal with Pseudomonas grown on culture and no response to topical treatments. A polypoid mass of granulation tissue has been found frequently at the juncture of the cartilagenous and membranous portion of the canal. The infection may progress downward or medially from its external canal origin and cause the complications of cranial nerve palsies (32 percent of Chandler's patients had facial nerve palsy), osteomyelitis of the skull, meningitis, parotitis, sigmoid sinus thrombosis, septicemia and death. The overall mortality has been 33 percent. Tomograms of the middle ear area may be helpful in showing if extension to bone, the mastoid sinuses or the middle ear has occurred.

Current suggestions regarding management include (1) early diagnosis whenever possible (determining extension of infection beyond the confines of the external canal), (2) early use of parenterally given carbenicillin and gentamicin if local measures are of no benefit (antibiotic alternatives include ticarcillin instead of carbenicillin and tobramycin or amikacin instead of gentamicin) and (3) early surgical debridement

if there is no improvement after the parenteral administration of antibiotics.

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Identifying the Gilbert Syndrome

REDUCED ACTIVITY of the enzyme responsible for conjugation of bilirubin is encountered in the very uncommon Crigler-Najjar syndrome and it is also encountered in the much more common Gilbert syndrome, probably the commonest cause of jaundice that you will encounter in your clinical practices. It occurs in something like 5 percent of the population and it is identified by demonstrating that the isolated increase in bilirubin seen on an SMA-12 is due to an unconjugated hyperbilirubinemia and not a direct hyperbilirubinemia. I had a patient referred to me yesterday who had been followed for six months as a case of hepatitis because they had failed to do the fractionation of a bilirubin and identify that it was an unconjugated hyperbilirubinemia present. So Gilbert syndrome is very common and needs to be identified because it is an entirely benign condition that requires no specific treatment.

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